Restricted

NAVY DEPARTMENT

BUMED NEWS LETTER

a digest of timely information

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Convalescence, Reconditioning and Physical Fitness: In a military hospital, as distinguished from a civilian hospital, convalescence is under the close supervision of a physician. The civilian patient tends to leave the hospital as soon as the acute phase of his illness is over. The military patient is not discharged until he is fit for full duty. However, in either case convalescence is often thought of in terms of time. For example, the question may be raised: how long after a lobar pneumonia should a patient be allowed up, be fit for limited duties about the hospital, be fit for duties about the grounds, and, finally, be fit for all of the duties that his position in the Navy may require of him?

Recently a meeting of the Committee on Convalescence and Rehabilitation of the National Research Council was held for the purpose of appraising the handling of convalescence. It was recognized that hypofunction of the body develops as a result of illness, and that this hypofunction is dependent upon the deleterious effect both of the morbid process itself and of the treatment; i.e., rest in bed, immobilization, medication, etc. The purpose of the meeting was to discuss the general problem of reconditioning the individual after illness and testing him

with regard to his physical fitness at various stages in his convalescence. Points of considerable interest were raised at the meeting and may be summarized as follows:

Physical fitness, which is concerned with strength and endurance, is not necessarily related to health, which is concerned with freedom from disease. Maximum physical fitness can be maintained only by a high level of regular physical exercise. When men accustomed to doing heavy physical work are assigned to tasks involving light physical work, their physical fitness promptly deteriorates. It is not surprising that a major illness reduces physical fitness, but it is surprising how much physical fitness is lost when a long minor illness necessitates rest as part of its treatment. Even a healthy individual used to heavy physical work confined for a few weeks to a hospital for study of suspected illness may require reconditioning before returning to his duties simply because he has been withdrawn from his normal physical activity.

A recent study made by physicians of the Army Air Corps of 600 cases of primary atypical pneumonia revealed that those patients who were started on a controlled reconditioning program in convalescence as soon as their sedimentation rates had returned to normal had, in general, a much shorter hospital stay than those allowed to take their convalescence into their own hands. In another experiment it was found, oddly enough, that when patients with limbs in casts vigorously exercised the body and uninjured limbs, the muscular atrophy under the casts seemed to be less.

Convalescence begins when the morbid process has run its course. Objective tests at present available to determine when the patient has reached this point are not always reliable, but in many types of illness the sedimentation rate is a useful aid. One of the results of prolonged rest in bed and of illness is loss of vasomotor tone with unsatisfactory response of the circulation to assuming the erect posture. Some of this loss of vasomotor tone can be avoided by elevating the head of the bed or using a "high Gatch" position as soon as the patient's condition will permit.

A curve of the results of repeated tests designed to estimate the efficiency of the vasomotor apparatus, such as the response of the pulse and blood pressure to changes in posture and to mild exercise is of value in estimating the patient's progress during convalescence.

In convalescence the patient's own impression of what he can do is almost worthless. Motivation plays a large role and is the most difficult factor to appraise. Everyone is familiar with the slow progress of the patient who is not anxious to return to his duties or even to remain in the Navy. Such an individual by "gold-bricking" retards his own return to physical fitness and may even influence adversely his scoring in tests of endurance and strength. All of the

members of the Committee agreed that in determining the point where convalescence begins and in evaluating the subsequent progress in early convalescence, clinical judgment is the final determining factor and of more importance than any available objective test.

Tests of physical performance may be of value as the convalescent patient approaches the time to return to duty. Here strength and endurance must be clearly differentiated. A man capable of exerting great physical effort for a short time may have little endurance in prolonged physical work. Endurance cannot be measured in terms of speed; for example, a work horse can never be made to go as fast as a race horse but may have much greater endurance.

It was generally agreed by the members of the Committee (1) that the withdrawal from accustomed physical exercise necessitated by illness results in striking deterioration in physical fitness, that this debilitation can be greatly increased by the effects of the morbid process itself, and that illnesses vary greatly in their disabling effect; (2) that rehabilitation by supervised exercise should begin as early in convalescence as is consistent with safety and that the point at which it should start is determined better by clinical judgment than by any available clinical tests; (3) that at times it is necessary to disregard the judgment of the patient himself as to what he can do; (4) that most patients during convalescence are benefited by a carefully and expertly supervised reconditioning program designed to restore them as rapidly as possible to maximum physical fitness; and (5) that such a program is well justified by its effect in reducing the number of sick days of military personnel.

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Intramuscular Injections of Oil: Emery and Matthews injected mazola, olive, cotton seed, sweet almond, sesame and peanut oils into the muscles of the hind legs of rats. Tissue capsules developed around the oil within a few days, forming oil cysts, some of which remained in the muscles for several months. Abscesses developed in nearly half of the rats injected with sweet almond oil and in a few of those injected with cotton seed oil. Sesame oil formed a more durable cyst wall than mazola, olive and peanut oils, but all four were less irritating than sweet almond and cotton seed oil.

When any one of the six oils was injected subcutaneously, the globule readily disseminated, cysts were infrequently seen at autopsy, and abscesses were never found. (J. Lab. and Clin. Med., Dec. '43.)

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Plaster of Paris Casts: Luck has made a study of plaster of Paris casts with special emphasis on determining those factors in the technic of applying

the plaster which make for strength or weakness. The following is the author's summary of the conclusions reached in his study:

"Immobilization by encasement in plaster of Paris is an indispensable part of the treatment of many war wounds and demands good plaster technic. Good plaster technic means rapid application of the cast, comfort and protection to the patient, the use of a minimum of plaster, and less difficulty in transportation.

"Plaster of Paris, a powder, transforms to crystals when mixed with water. In the crystalline state it depends principally on compact interlocking of the crystals for its rigidity and strength.

"The 'critical point' is that time in the setting process when the plaster crystals interlock and give the cast rigidity and strength. Movements of the cast, such as changes of alignment and molding after the critical point in the setting process, mean impairment of the ultimate strength of the cast. The later after the critical point the cast is manipulated, the greater will be the damage. Of the defective casts analyzed, more had been impaired by manipulation after the critical point than by any other single cause.

"Detection of the critical point requires practice and varies with different brands of plaster, but in general it is that point when the plaster is of the consistency of thick cream and begins to lose its wet glistening character. When the appearance of the plaster has become dull and the cast is becoming firm, the critical point is passed.

"Lamination of casts occurs when one layer of plaster-crinoline dries before another is applied, preventing fusion of adjacent layers. When fresh plaster is wrapped over a dry plaster surface, the dry surface should first be roughened by scratching it with a sharp knife. This is necessary when casts have to be applied in segments, e.g., a cylinder for a shaft fracture of the tibia and fibula, then the foot portion, then the thigh portion.

"Most plaster of Paris and crinoline now available are good. More unsatisfactory casts are the result of poor technic of application than of defective plaster of Paris and crinoline. To overcome bad technic of application, a great excess of plaster is frequently used. The use of two or more times the required number of plaster rolls and splints is often observed.

"A cast does not attain its full strength until the water within it in excess of that needed for 'water of crystallization' evaporates. This process may require several hours for small casts and several days for large ones. Arrangements for air to circulate around the cast until it dries are important. If a large,wet cast is kept covered with heavy bed clothing, the cast may lose its

rigidity and become rubbery and useless. This is true especially in humid climates.

"The use of such materials as sugar to retard the setting time and salt or borax to accelerate the setting time should be avoided under most circumstances. Cold water effectively retards the setting time, and warm or hot water accelerates it. Varying the temperature of the water and the length of the soaking time are usually adequate to regulate the setting time. Water at a temperature of 70 to 95° F. and a soaking time of about one minute are ordinarily employed.

"In the defective casts analyzed, more painful points resulted from friction beneath thickly padded casts than resulted from pressure when little or no padding was used. When no padding is used a plaster splint is best applied anteriorly and posteriorly before applying the plaster bandages. The bandages should be 'laid on,' never 'drawn on.'

"With reinforcing casts that encase the ankle, knee, elbow and wrist, the reinforcement should be placed front and back and not on the sides. Major reinforcement for the shoulder in shoulder spicas should be over the top of the shoulder and in the axilla; for hip spicas reinforcement should be placed anteriorly, posteriorly and laterally, with the strongest reinforcement laterally.

"Splints contribute more to the strength of a cast when they are thick and narrow than when they are thin and wide. Non-plaster splints should be perforated or notched in order to key them into the cast.

"When plaster splints and slabs are used alone and not incorporated in a cast, the rules for their application are opposite in two respects to their use in casts. In immobilizing joints moving predominantly in one plane, such as the knee and elbow, splints or slabs used alone are stronger when they extend well up on one or both sides or are used exclusively on the sides. Further, they are better used thin and broad, rather than narrow and thick." (J.A.M.A., Jan. 1, '44.)

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Salt Water in the Galley: Sea water is commonly used on ships for scrubbing decks, including galley and compartment decks, and for cleaning the potato-peeling machine. This practice is regarded as safe when far out at sea, but it is unsafe when in polluted harbors.

Article 1324 Navy Regulations states: "In ports where cholera, typhoid, dysentery, or other water-borne diseases are prevailing, either sporadically or epidemically, the use of harbor water shall not be permitted on board either upon or below the upper deck; also, in ports where the water is contaminated by sewage, animal matter, or refuse, its use shall only be permitted after consultation with the medical officer of the ship."

Not infrequently, through the carelessness of those detailed to the supervision of scrubbing the galley, a change from salt to fresh water is not made upon arrival in port.

It has been observed that water from a hose used in connection with scrubbing the decks in the galley may splash to a height of 4 or 5 feet, spraying utensils, tables and foods.

It is believed that the surest way to eliminate this hazard is to discontinue the use of salt water for any type of cleaning in the galley. (Contributed by Comdr. C.B. Stringfellow (MC), USN.)

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Acute Appendicitis: The first two papers in the January issue of the U.S. Naval Medical Bulletin are concerned with the problem of acute appendicitis.

In civil as well as military practice it is a generally accepted principle that when a diagnosis of acute appendicitis is established and there is available a competent surgeon as well as adequate facilities for surgery, immediate operation represents the conservative and statistically safe procedure, while failure to operate may involve serious hazards for the patient.

Situations may be encountered, especially by corpsmen on independent duty, in which a competent surgeon or adequate facilities are not available, and in which operative intervention may be the less conservative approach to the problem. Irwin and Coates discuss this aspect of the matter as follows:

"The problem of handling acute appendicitis at sea has received wide publicity through the radio and the press as a result of appendectomies having been performed by enlisted personnel. We believe more lives will be lost through surgery performed by unqualified persons than would be lost through a policy of delay of surgery, using proper treatment during the delay period."

The authors believe that many factors should influence the decision whether or not to operate. Among these are "operating room facilities, equipment, skill and experience of the medical staff, the weather, condition of alert or nearness to battle."

Non-operative treatment does not, however, imply doing nothing. It involves an active and intelligent use of every available means of combatting the infection short of operation.

Irwin and Coates recommend (1) morphine every 4 hours, (2) Fowler's position, (3) no food by mouth, (4) the liberal use of parenteral fluids and (5) the administration of sulfonamides by mouth or intravenously.

Berkely and Watkins in the same issue of the Bulletin describe their experience with the conservative treatment of acute appendicitis on a transport. Eight cases diagnosed as acute appendicitis were given sulfathiazole by mouth. Liquids by mouth were not forbidden. "The symptoms and findings remained the same in some cases and in others became more pronounced for the first 12 hours. All cases showed a progressive diminution of pain, tenderness and rigidity after the first 12 hours. There was also a progressive decrease of the white blood cell count to normal."

The success of Berkely and Watkins in their small series of cases emphasizes the fact that in many patients well treated short of surgery, the acute inflammatory process will subside without perforation. Past experience with this condition, however, would lead one to expect that observation of a larger series would demonstrate that a certain number of patients will go on to perforation and develop peritonitis in spite of non-operative therapy including the use of sulfonamides. Local conditions such as obstruction of the lumen of the appendix with rapid formation of pus under pressure may be a deciding factor. Irwin and Coates point out the value of the Levine or Miller-Abbott nasal tube and the Wangensteen type of suction, and these devices for intestinal decompression may be lifesaving when, in operative therapy, the necessity for which has been dictated by circumstances, peritonitis develops.

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Penicillin in the Treatment of Relapsing Fever: Relapsing fever has a wide geographical distribution. Epidemics of the louse-borne variety (Borrelia recurrentis) have occurred within the last 25 years in Eastern Europe, Northern Asia, India, China, Western Asia, and in North and Equatorial Africa. Since 1934 the chief foci have been Africa and Russia. The tick-borne variety (Borrelia duttoni) tends not to spread but to remain localized in areas corresponding to the distribution of its tick-vectors, the soft ticks of the genus Ornithodorus. Foci are recognized in Africa, Asia, Europe, Canada, Central America, South America, and in the United States in the states of Texas, Colorado, Oklahoma, Kansas and California.

As naval personnel have been operating in many of these areas, it reflects credit on our measures of sanitary control that only two new cases of the disease have been reported to the Bureau during the past year.

Excellent and brief outlines of the two types of relapsing fever are given in the most recent edition of "Notes on Tropical and Exotic Diseases of Naval Importance" prepared at the Naval Medical School. Neoarsphenamine in the therapy of relapsing fever is recommended.

Heilman and Herrell (Proc. Staff Meet., Mayo Clin., Dec. 1, '43.) have recently studied the control by penicillin of experimental overwhelming infections in mice caused by Borrelia novyi, a strain of the organism of relapsing fever which is louse-borne and has been recovered from some cases in North

America. Of 28 untreated mice, 75 per cent died. Of 26 treated mice, only one, or 4 per cent died.

While these experiments do not assure the achievement of a similar therapeutic result in man, they suggest the wisdom of experimental trial of penicillin in relapsing fever in man where the drug is available.

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Louse Control: Chlorinated Diphenyl Ethane: Louse control discipline and good personal hygiene are of great importance in the prevention of louse infestation. Frequent talks to the men are of value regarding the dangers from lice and the methods of keeping themselves rid of them. Ample laundering and bath facilities should be provided where possible and frequent inspections should be made of personnel and clothing to detect the presence of lice, special attention being given to the seams of the innermost clothing. Running a heated flat-iron over the seams will destroy ova.

A new powder has been issued (S13-451) which is highly effective in louse control. The active principle is 2,2-bis (p-chlorophenyl)-1,1,1-trichloroethane, sometimes called Dichloro Diphenyl Trichloroethane, or D.D.T. or "gesarol." Clothes may be dusted with it whether they are on the person or not.

A plunger-type hand duster or a compressed air powder duster is satisfactory for application of the powder to clothes the removal of which is not practicable. The powder should be blown under the innermost layers of the clothing, care being taken that every part is reached and that the seams receive special attention. Two ounces of the powder are sufficient for this procedure. The application need be made only every two weeks to a month, provided the individual does not change his clothing or bathe, but must be repeated after laundering clothes.

Dusting by hand requires a little over an ounce of the powder. It should be rubbed into the seams, especially the inner folds of the seams. When properly applied by spray or by hand, all lice and eggs will be killed within 48 hours.

This powder containing D.D.T. applied to the hairy parts of the body will protect against and exterminate all types of lice and "nits." In addition it can be used for other clothing and bedding, especially since it is effective also against chiggers, fleas and bed bugs.

Experiments being conducted at the present time indicate the possibility of impregnating underwear and other clothing with a 1 per cent emulsion of chlorinated diphenyl ethane. The results to date make it appear that underwear so impregnated remains louse-free for about eight weeks despite ten

washings and frequent exposure to lice. Adoption of this method of using D.D.T. will have to await the results of further field trials.

Chlorinated diphenyl ethane has an advantage over steam and methyl bromide fumigation in that it has persisting prophylactic value against re-infestation and is simpler to use. Although non-irritating and nontoxic when used externally, this substance is poisonous when ingested in sufficient quantity. Proper precautions should be taken to avoid its getting into food. (C.P.K.)

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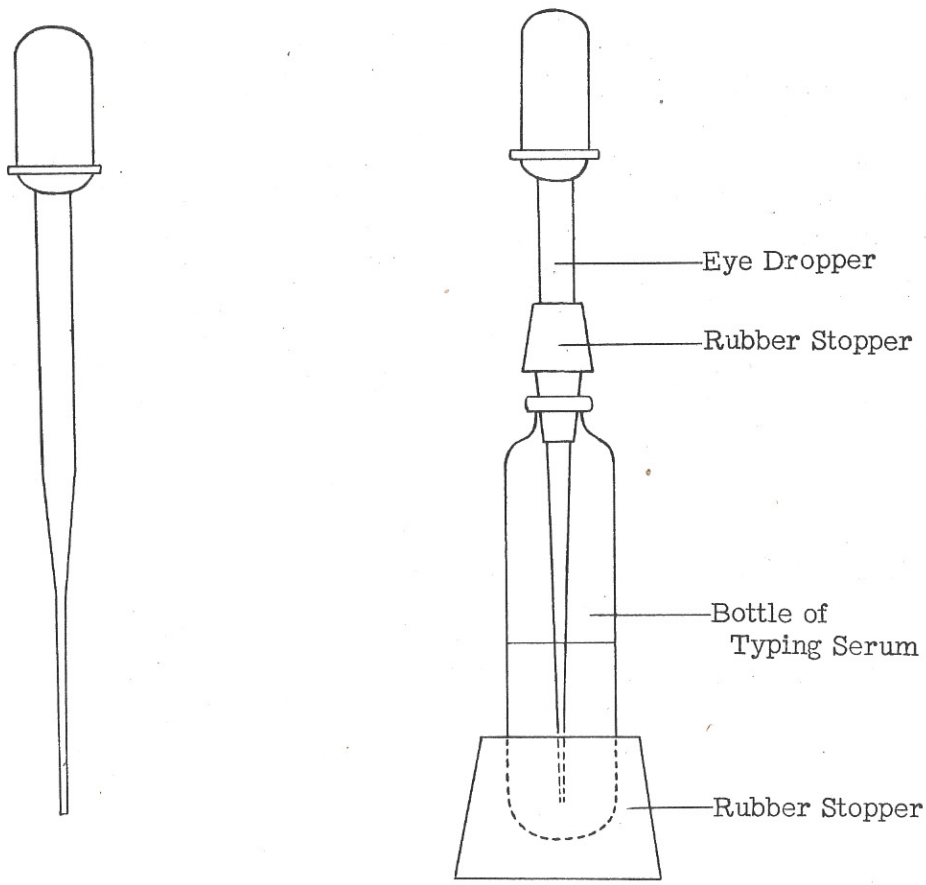
Preservation and Dispensing of Typing Serum: The diagrams below show the method used at the U.S. Naval Hospital, Memphis, Tennessee, in storing and dispensing working typing sera. The rubber stopper that comes with the serum is punctured and a glass eye dropper that has been drawn out under heat is inserted. According to Benjamin the advantages are: that no serum is discarded; that the container is always stoppered; that no extra equipment is necessary; and that the serum is kept clear and uncontaminated. (H.B. Benjamin, Lt. Comdr. (MC), USNR.)



Influenzal Immunity: That the immunity against reinfection conferred by a single attack of mild influenza may be short-lived is suggested by some experimental work reported by Francis at the last American Public Health Association meeting. He inoculated a number of human volunteers with Influenza B virus. A considerable number of those inoculated had mild attacks of influenza. When those who contracted influenza were reinoculated with the same virus four months later, a significant number of them again contracted the disease, although in milder form.

This experimental work, while of much interest, is not entirely in accord with knowledge of immunity to influenza gained through the study of the behavior of this disease when it occurs in epidemic form. When influenza is highly epidemic, one must expect that, at least among city dwellers, exposure is almost universal, and yet it is common experience that certain individuals escape the disease. The nature of this immunity is not understood, as many of the persons spared give no history of the disease. Even if one presupposes that those who do not contract the full-blown disease have influenza in a subclinical form, it is still difficult to escape the conclusion that they have greater resistance to it than those who become more acutely ill

The following passage is taken from the Annual Report of the Surgeon General of the Navy for the year 1919:

".....many men of the Navy who had influenza in the spring or summer of 1918, while in European waters, escaped during the later epidemics (winter 1918-1919) both in Europe and the United States. The British Grand Fleet experienced the same thing; with few exceptions those men who contracted influenza in May and June were not attacked during the more fatal epidemics in October, November and December. The conclusion is that mild attacks earlier in the year, as a rule, conferred immunity against the more fatal type of the disease which prevailed subsequently."

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Analysis of Dried Plasma Reports: A statistical analysis of 1,407 completed questionnaires on administration of the Standard Army-Navy Package of Dried Plasma has been completed. It is of interest to compare the report of this analysis by the Naval Medical Research Institute (Report No. Two - Project X-179) with the preceding report analyzing 1,751 administrations of liquid plasma, a summary of which was presented in the Bumed News Letter of August 20, 1943.

The total number of untoward reactions from dried plasma was 74 (5.3 per cent). This compares with 4.1 per cent for liquid plasma as a whole, 5.6 per cent for liquid plasma under 4 months old and 3.0 per cent for liquid plasma over 4 months old.

Despite the fact that 31 per cent of the dried plasma administrations were outside the continental limits, the distribution of indications for giving the plasma, the relation of indications to untoward reactions, the per cent of beneficial results, the distribution of dosage and the time of day when the plasma was administered were remarkably similar to those of the liquid plasma study. The average amount given each patient was less for dried plasma (526 c.c.) than for liquid plasma (711 c.c.). It is seen, however, that the change to the new large size package containing 500 c.c. of original plasma is easily justified. The incidence of urticarial reactions from dried plasma was double that from liquid plasma.

Twenty-five (3.0 per cent) of the 734 patients involved were reported to have died during the course of plasma therapy. Twenty-two of these patients were receiving plasma following trauma. Although in the series as a whole, hypoproteinemia was the most frequent indication for therapy, only two of the patients who died were receiving plasma for this reason.

Among the products of the various biological laboratories manufacturing the dried plasma package, there were no significant differences in untoward reaction rate.

All medical officers are urged to complete the questionnaire accompanying each package of plasma or albumin and to return it to the Blood Research Division, National Naval Medical Center, Bethesda, 14, Maryland, in order to increase the validity of these statistical analyses the results of which are used in planning the future program. (E.L.L.)

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Malaria Control and the Construction Battalions: By authority of the Secretary of the Navy, March 1943, Sanitary Sections for the control of malaria were set up in Construction Battalions, both those within the continental United States and those in malarious areas outside the continental limits.

This program has already begun, and in May 1943 at the Construction Battalion Training Center, Camp Peary, Virginia, special courses were started for personnel of Sanitary Units. Since that time, more than 1,000 men have been given basic indoctrination in malaria control.

Each Sanitary Section of the Construction Battalion consists of ten petty officers and one hundred men. All officers in the Battalion and petty officers and men in the Sanitary Section are given intensive lecture courses and field demonstrations. In addition, all rated men are given further training for three weeks in basic procedures of mosquito control. Members of this group are the actual directors of field work in the malarious areas. Of this group, usually three who show a special aptitude are given an additional three weeks work in

methods of mosquito survey and identification. They are then in the position to assume more technical responsibilities and to carry on in case the Battalion becomes separated from its parent unit.

It is hoped that Malaria Control Officers will take advantage of this available source of trained personnel. (T.J.C.)

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A New Microfilm Viewer: Medical officers are reminded that microfilm copies of papers in current or filed medical journals, either American or foreign, may be obtained from the Army Medical Library. This service is available to Naval medical officers without charge. Requests should be addressed to Photoduplication Service, Army Medical Library, Washington 25, D.C. The name of the desired journal together with the year and volume number, title of paper and initial and final page numbers, if possible, should be given. Since the announcement of this service in the Bumed News Letter of June 11, 1943, many medical officers in the Navy have availed themselves of this privilege.

A microfilm viewer has been put into quantity production. It will be sent on approval to all medical officers outside the continental limits of the United States who request microfilms from the Photoduplication Service. Medical officers within the continental limits may obtain viewers by writing to the Photoduplication Service. The price is $3.75; this is the amount the Army Medical Library transmits to the manufacturer. The Library simply acts as an intermediary in getting the viewers promptly into the hands of those who need them.

The viewer is provided with a space for the film which is large enough to receive a kodachrome or other pictorial slide. This will enable the manufacturer to offer it to the general public at a later date through photographic supply dealers. Thus a sufficiently large market will be reached to permit an eventual lowering of the price.

It is adapted especially to the needs of those in isolated places who wish to make the literature pertaining to their work available for leisurely study.

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Mecholyl: The use of mecholyl (acetyl-B-methylcholine) in paroxysmal tachycardia was discussed in a paper by Morgan which appeared in the Annals of Internal Medicine of November 1943 and which was abstracted in the Bumed News Letter of December 24. It was not sufficiently emphasized in this abstract that mecholyl should be injected subcutaneously and never intravenously.

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Reports on Research Projects at the Naval Medical Research Institute Available for Medical Officers:

X-127 The Tablet Emergency Ration for Lifeboats, Rafts and Floats.

X-184 Losses of Vitamin C in the Preparation of Certain Foods.

NMRI-20 Chemical Analysis of Food Containers Submitted by the Quartermaster; U.S. Marine Corps.

NMRI-29 Evaluation of the Data Related to the Revision of the American Optical Company's Pseudo-Isochromatic Plates for Testing Color Vision.

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Public Health Foreign Report:

Disease	Place	Date	Number of Cases
Plague	Indochina (Cochinchina)	Sept. 21-30, '43	1
Smallpox	British East Africa	Oct. 16-23, '43	134
	British Honduras	Nov. 13-20, '43	1
	Guinea (French)	Oct. 11-20, '43	34 (4 deaths)
	Indochina	Sept. 21-30, '43	78
		Oct. 11-20, '43	97
	Sudan (French)	Oct. 11-20, '43	110 (4 deaths)
	Turkey	September '43	524
Typhus Fever	Greece	Year 1942	405
	Hungary	Oct. 17-30, '43	10
		Nov. 1-13, '43	20
	Rumania	Oct. 8-15, '43	84
	Slovakia	Oct. 17-30, '43	12
		Oct. 31-Nov. 6, '43	12
	Turkey	September '43	72
Yellow Fever	Portuguese Guinea	Nov. 10, '43	(Outbreak)

(Pub. Health Reps., Dec. 3 & 10, '43.)

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Availability of Materials for Transfusion Therapy: Because of numerous inquiries from medical officers regarding the availability and the means of obtaining materials for transfusion therapy, the following table presenting information on procurement has been drawn up:

Materials for transfusion therapy	Obtainable from	Naval Medical Activities			
		All	Afloat and beyond continental limits	Afloat and beyond continental limits where space is at premium	Within continental limits
Standard Army-Navy Package of Dried Plasma (300 c.c.)	Naval Medical Supply Depots		Available	Available	
Standard Army-Navy Package of Dried Plasma (600 c.c.)	Naval Medical Supply Depots		Available	Available	
Standard Army-Navy Package of Human Serum Albumin (Concentrated)	Naval Medical Supply Depots			Available	
Liquid Citrated Plasma (300 c.c.)	Naval Medical School				Available
Liquid Citrated Plasma (600 c.c.)	Naval Medical School				Available
Equipment for indirect whole blood transfusion and preservation	Naval Medical Supply Depots	Available	Available	Available	Available
Equipment for direct whole blood transfusion	Open purchase	Available	Available	Available	Available
Equipment for plasma prepation and preservation	Open purchase	Available	Available	Available	Available

(L.R.N. & E.L.L.)

BUMED-X-FEW-III
L8-2/JJ57(042-43)

7 Jan 1944

To: All Medical Officers.

Subj: Letter of Information and Instruction on the Use of Penicillin.

Refs: (a) Letter of Information and Instructions on the Use of Penicillin. L8-2/JJ57(042), 5 Jul 1943.
(b) Medical Stores, penicillin. L8-2/JJ57(042-43), 7 Jan 1944.

I. Reference (a) is herewith modified and superseded.

II. Distribution of Penicillin: The body of reference (b) is quoted herewith:

"(1) Penicillin has been added to the Supply Catalog as follows:

Stock No.	Item	Unit
S1-1130	Penicillin, sodium, crystalline, 100,000 Oxford units in ampule (5 ampules in box) (potency 3 months)	Ampule

(2) Issues of limited stocks available have previously been specifically rationed. Recent production expansion has resulted in increased quantities being allocated for Navy use. Effective 1 February 1944, specific rationing of penicillin will be discontinued.

(3) Penicillin is now carried in stock at NMSD, Brooklyn, N. Y. only. When anticipated increase in deliveries permit, stock will be carried at NMSDs, Oakland and Pearl Harbor, T. H. It is not expected that available production will permit stocking of penicillin at other Naval Medical Supply Depots or Storehouses, particularly in view of the short potency period.

(4) After 1 February 1944, penicillin will be issued on NavMed Form 4 requisition, or despatch request when urgency warrants, to BuMed (Materiel Division, Brooklyn), for the treatment of those conditions for which the drug is known to be effective. Such requisitions or requests shall contain a concise statement as to the urgency of the need, to enable decision as to priority of issue in the event stocks are inadequate to fill all requests. Quantities requested shall be limited - to not more than one (1) month's requirements.

(5) Penicillin on hand at any activity, which prospectively cannot be utilized within potency dating shall be reported as excess, by air mail or despatch to BuMed (Materiel Division, Brooklyn), not less than two (2) weeks prior to

expiration dating. Such material will be ordered transferred to the nearest activity prepared to use it."

III. The Source and Nature of Penicillin: Penicillin is an antibiotic agent which is produced by the mold, Penicillium notatum, when cultivated on suitable media and under certain conditions. It is extracted from the medium, purified, dried, tested for pyrogens and sterility, and packaged in sterile ampoules under aseptic conditions. At present it is supplied as the sodium salt, which is a fine powder varying in color from light yellow to dark brown. Other salts of penicillin may be available later.

IV. Storage and Stability: The dried powder, when contained in ampoules, is quite stable at ordinary room temperature, but high temperatures and prolonged exposure at room temperature cause significant deterioration. To assure maximum potency, the ampoules should therefore be stored in refrigerators. Though the penicillin expiration date is based upon preservation of penicillin at ordinary refrigeration temperatures (+ 4°C.), freezing temperatures will prolong the duration of potency. In the storage of penicillin, freezing temperatures may be used to advantage by the placing of penicillin in frozen meat and food compartments, when these are available. In liquid form penicillin is extremely unstable. Solutions should therefore be made up preferably just before administration, or at least daily and then kept under refrigeration at about + 4°C.

Penicillin, like many other biological products, loses its potency gradually, thus a particular lot may represent a gradually decreasing percentage of the stated potency, after the expiration date.

V. Preparation for Administration: The crystalline penicillin contained in ampoules, 100,000 units per ampoule, is sterile. It is extremely soluble and may be dissolved in sterile, distilled pyrogen-free water, normal saline or 5 per cent dextrose solution. Additional sterilization is not necessary, and must not be done since heating destroys the potency of penicillin. Occasionally small particles of insoluble material may be present. These can be removed by passing the solution through sterile filter paper or a filter which is part of an intravenous set.

A. Intravenous solutions:

1. For single or interrupted injection, dissolve the dry powder in sterile normal saline in concentrations of 1,000 to 5,000 units per c.c.

2. For continuous intravenous injection, use a low concentration of 20 units per c.c. in normal saline or 5 per cent glucose solution.

B. Intramuscular Injections: A suitable volume is obtained by using a concentration of 5,000 units per c.c. of normal saline.

C. For topical application prepare a solution containing 250 units of penicillin per c.c. of normal saline.

D. For intrathecal injection a concentration of 1,000 units per c.c. of normal saline is recommended.

VI. Methods of Administration: Penicillin is excreted rapidly in the urine, therefore, it is usually necessary to administer large amounts at frequent intervals to maintain an effective blood level. The most efficient and economical means of accomplishing this result is by continuous intravenous administration at a constant rate or by frequent intramuscular injection (every 3 hours) throughout the 24-hour period.

A. Intravenous:

1. Single injections of a solution containing 1,000 to 5,000 units per c.c. is recommended only in those instances in which it is desirable quickly to establish an effective concentration of penicillin in the blood. As penicillin is very rapidly excreted, much is wasted by this method of administration. Continued therapy should then be with either the intramuscular or constant intravenous methods.

2. Continuous Intravenous: A concentration of 20 units per c.c. (20,000 units-liter of normal saline) is recommended with an injection rate of 30 to 40 drops per minute. Average daily dose by this route: 3 liters or 60,000 units.

B. Intramuscular: 1 c.c. to contain 5,000 units in normal saline. 15,000 units (3 c.c.) are given intramuscularly every 3 hours day and night. It is imperative that injections be given promptly according to schedule in order to maintain a continuously effective level.

C. Topical: Penicillin - 250 units per c.c. normal saline is applied on compresses. Small Dakin tubes are inserted in the compresses and additional amounts of penicillin are administered through tubes every eight hours. It is imperative that penicillin be trapped at site of lesion for a minimum period of 6 to 8 hours. Penicillin cannot be used effectively by irrigation.

D. Intrathecal: Penicillin, in concentration of 1,000 units per c.c. normal saline, is injected intrathecally every 12 hours. Dose is 10 c.c. or 10,000 units every 12 hours.

E. Local Injection: Penicillin, in concentration of 5,000 units per c.c. normal saline, may be injected into an empyema cavity, a joint cavity, or an abscess cavity, in varying doses (20,000 to 40,000 units depending on size of cavity). In brain abscess - strength is diluted to 1,000 units per c.c.

Recent experience suggests that combined methods of penicillin administration may often be used to advantage. In cellulitis, osteomyelitis, purulent arthritis, empyema, brain abscess and meningitis, penicillin should be administered locally as well as systemically.

The administration of penicillin intrathecally, in concentration of 1,000 units per c.c., is attended by no untoward reactions, such as pleocytosis.

The hazard of penicillin-fastness dictates intensive and effective initial dosage for all infections.

VII. General Indications for Use: Penicillin should not be used in infections with organisms known not to be susceptible. The known-susceptible organisms are most of the gram positive cocci and bacilli and the gram negative diplococci. The most important organisms in this group against which penicillin has proven effective are: the pneumococcus, streptococcus, staphylococcus, gonococcus, meningococcus and Cl. welchii.

Penicillin has no effect against the gram negative bacilli and may be inhibited in its action upon other susceptible organisms by some gram negative organisms when present in mixed infection. Among the insusceptible organisms are H. influenzae, typhoid-dysentery-colon organisms, pyocyaneus (pseudomonas) and Friedlander's bacillus (K. pneumoniae).

Penicillin has also proven ineffective in infections with the Monilia, the tubercle bacillus and in malaria.

Penicillin has not been found to be effective in the treatment of subacute bacterial endocarditis.

Preliminary reports of research in the penicillin therapy of syphilis are very promising. However, it is desired that penicillin not be used in the treatment of syphilis in the Navy without specific authorization of the Bureau of Medicine and Surgery.

This reservation is dictated by the fact that, while clinical healing of lesions and reversal of serology may be brought about, only continuous observations over an adequate period of time will establish the result as a cure. It is, therefore, planned to reserve all penicillin treatment of syphilis in the Navy to the U.S. Naval Hospital at Bethesda, Maryland, for this research period.

VIII. Specific Indications for Use and Recommended Dosage: In order to effect the maximum utilization of the quantities of penicillin available, a judicious selection of cases should be exercised. In general, sulfonamide-resistant infections should receive first consideration. The dosages and methods of administration presented in the following paragraphs are based upon experience in the use of the drug and are suggested as a guide for the introduction of penicillin therapy. As the field of application is broadened, the results of future experience will undoubtedly necessitate changes in these recommendations.

A. Serious infection with bacteremia due to penicillin-susceptible organisms:

1. Total dosage: 1,000,000 to 3,000,000 units.

2. Duration of treatment: 7 to 14 days.

3. Method:

(a) Continuous intravenous injection at a rate of 5,000 to 10,000 units per hour; or

(b) Intramuscular injections of 15,000 to 30,000 units every three hours day and night.

4. It is imperative, in the acute fulminating infections involving streptococcus and other penicillin-susceptible organisms, that penicillin be given intravenously, intramuscularly, and, where possible, locally. Parenteral dosages of 100,000 to 200,000 units daily are usually necessary in these cases. Severe staphylococcic infections may require 200,000 to 400,000 units daily.

Failure of the infection to respond in 36 to 48 hours necessitates re-examination for contained pus or infections not susceptible to the action of penicillin. The action of penicillin is enhanced by early, adequate surgical drainage.

B. Septic Compound Fracture, Infected Wounds and Osteomyelitis:

1. Total parenteral dosage: 1,500,000 to 2,500,000 units.

2. Duration of treatment: 14 to 21 days.

3. Method of administration:

(a) Intramuscular injections of 15,000 units every 3 hours day and night, and

(b) Topical application of penicillin solution containing 250 units per c.c. every 8 hours, combined with adequate surgical drainage.

4. When susceptible organisms predominate in the wound, there is prompt improvement during treatment. Later recurrence of infection often occurs and usually indicates the presence of sequestra or foreign bodies requiring surgical intervention. Evidence is accumulating that surgical intervention is often necessary in penicillin therapy of acute staphylococcic osteomyelitis of the long bones, whereas, a more conservative program is warranted in infections of the flat bones.

C. Meningitis: due to streptococcus, staphylococcus and pneumococcus.

1. Total dosage:

(a) Intrathecal: 40,000 to 60,000 units.

(b) Intramuscular: 800,000 to 1,000,000 units.

2. Duration of treatment: 7 to 10 days.

3. Method:

(a) Intrathecal administration of 10,000 units every 12 hours for 3 to 4 days, then reduction of dosage to 5,000 units every 12 to 24 hours for an additional 3 to 5 days.

(b) Intramuscular injections - initial dosage, 30,000 units every 3 hours to be followed upon favorable response by doses of 15,000 units every 3 hours for 7 to 10 days, given in combination with the intrathecal administration.

4. Penicillin is effective in the treatment of meningococcus infections but, because of the effectiveness of sulfadiazine, should not be considered the agent of choice except in the very fulminant cases, and in those cases of usual severity which do not respond to sulfadiazine. In those severe fulminating cases, characterized by bacteremia, severe purpura and circulatory collapse, it is strongly recommended that penicillin be administered in combination with sulfadiazine in addition to the indicated supportive measures.

D. Sulfonamide-resistant gonococcus infections: A gonococcus infection may be considered to be sulfonamide resistant if cultures or smears remain positive after two courses of sulfathiazole or sulfadiazine, each course consisting of a minimum of 20 Gm.

1. Total dosage: 100,000 units.

2. Duration of treatment: 5 doses.

3. Method of administration:

(a) Intramuscular injections of 20,000 units every 3 hours for 5 doses.

4. With this procedure approximately 100 per cent cures have been obtained. Experience has shown that in cases of sulfa-fast gonococcus infections treated with 50,000 units, approximately 15 per cent failures result. This necessitates re-treatment with 100,000 units. Where the dosage is limited to 80,000 units, there is a smaller percentage of failures.

Though a saving of penicillin could be effected by using 50,000 units as the initial course of treatment, even when the 15 per cent failures are retreated with an additional 100,000 units, the effective man-hours gained, under present conditions, is the more important issue. For this reason the initial 100,000 unit dosage, which best accomplishes this result, is recommended for general use.

E. Pneumococcus pneumonia:

1. Total dosage: 200,000 to 400,000 units.

2. Duration of treatment: 5 days.

3. Method of administration:

(a) Intramuscular injections of 5,000 to 10,000 units every 3 hours day and night for 5 days; or

(b) Continuous intravenous injection at a rate of 2,000 to 4,000 units per hour.

4. Complications, such as empyema, endocarditis, pericarditis or septicemia, will require more intensive and prolonged therapy.

F. Cellulitis:

1. Total dosage: 300,000 to 500,000 units.

2. Duration of treatment: average of 7 days.

3. Method of administration:

(a) Intramuscular injections of 15,000 to 30,000 units every 3 hours day and night; or

(b) Continuous intravenous injection at a rate of 2,000 to 4,000 units per hour.

(c) Topical application of penicillin solution (250 to 1,000 units per c.c.) in event of surgical drainage.

G. Maxillary sinusitis and chronic otitis media:

1. Total dosage: An average total dose of 6,000 to 8,000 units has been found effective.

2. Method of administration:

(a) Topical application of penicillin solution containing 250 units per c.c.

3. Where extension of infection results in cellulitis or osteomyelitis, the plan of therapy described for these conditions should be followed.

IX. Laboratory data recommended:

A. To be obtained on admission and repeated weekly:

1. Complete blood count.
2. Hematocrit.
3. Sedimentation rate.
4. Total serum protein.
5. Blood urea or N.P.N.

B. To be obtained daily:

1. White blood count and differential.
2. Urinanalysis.
3. Blood culture.

C. Smear and Culture: To be obtained before starting penicillin therapy and repeated as indicated by the course of the infection. The offending organism should be known in all cases. In mixed infection such as occurs in wounds, cultures will show disappearance of the susceptible organisms while the non-susceptible organisms may persist. These organisms, if pathogenic, must be attacked by other forms of therapy.

An example of this is the persistence of pyocyaneus (pseudomonas) in wounds, resulting in continued profuse discharge. However, its presence, after other susceptible organisms have disappeared, has often not interfered with rapid healing of such wounds.

X. Suggested additional procedures: Careful observation of fluid intake and output, maintenance of a positive nitrogen balance and control of secondary anemia associated with infection, enhance the action of penicillin and reduce the duration of morbidity. The use of repeated transfusions of whole blood, resuspended RBC, or blood plasma and infusions of amino acid preparations, where indicated, is recommended.

XI. Untoward Effects: Increasing experience leads to the conviction that certain untoward reactions are peculiar to particular batches of the drug, and are attributable to toxic impurities rather than to the active penicillin fraction. Deeply colored penicillin, which foams during preparation or which contains a nonfiltrable residue, is most apt to give reactions.

A. The reactions associated with particular batches of penicillin and thought to be due to impurities are:

1. Chills and fever.
2. Eosinophilia of 20 to 30 per cent.
3. Burning pain at the site of the intramuscular injection during the first 48 hours of treatment, but not thereafter.
4. Headache.
5. Faintness and flushing of the face.
6. Unpleasant taste after parenteral injection.
7. Tingling in testes.
8. Muscle cramps.

These reactions are being rendered less frequent by improved methods of production and Federal Laboratory control designed to eliminate toxic and pyrogenic lots of penicillin.

B. The following reactions have not been limited to particular batches and may be considered related to penicillin per se:

1. Urticaria:

Urticarial reactions have been noted in approximately 5 per cent of the cases. This reaction may occur after the first dose or as long as 19 days after the last dose.

2. Fever:

Elevations of temperature to 101° may occur in association with urticaria or separately. Elevation to 103°, associated with abdominal cramps, is occasionally observed.

These reactions suggest a form of sensitization analogous to the syndrome of serum sickness. However, sensitivity tests are negative and there is no evidence of permanent sensitization.

Treatment can usually be continued through the three to five-day period of urticaria with subsidence of the reaction.

3. Thrombophlebitis:

This reaction occurs frequently at the site of constant intravenous injections and may be accompanied by chills and fever if therapy is continued through the same vein. This complication can be avoided by the use of dilute solutions of penicillin and a daily change of the position of the needle.

4. Transient azotemia:

Minor degrees of azotemia (N.P.N. 40 to 45 mgm. %) have been reported during the course of penicillin therapy.

Albuminuria has not been observed and no clinical significance is attached to these lesser degrees of non-protein-nitrogen retention.

XII. Records and Reports: In order to gain the much needed additional information on the efficacy, probable shortcomings, and possible dangers of this drug, it is highly desirable that adequate case records be kept and that the data of these records be made available to all medical officers. This can best be done by summaries or brief articles submitted to the Bureau of Medicine and Surgery for publication in special letters, Bumed News Letter or the Naval Medical Bulletin, according to the nature and extent of the articles. The record of each case should therefore obviously include at least the following data:

1. A brief pertinent history of the illness.
2. The diagnosis with supporting clinical and laboratory data.
3. Dosage and methods of administration of penicillin.
4. Therapeutic result with the necessary laboratory evidence of success or failure.
5. Untoward effects and difficulties in administration, if any.

In addition to the special articles referred to above, there shall be submitted to this Bureau a routine monthly report which shall contain the information outlined in the form below, and in addition any other data that may be helpful in the evaluation of this drug.

SUMMARY OF CASES TREATED FOR THE MONTH OF....

Diagnosis	No. Cases	Av. Total Dose	"Success"	"Failure"

Those hospitals which have been forwarding individual case reports to the Bureau of Medicine and Surgery for statistical analysis are requested to continue their program until change in procedure, to attain certain research or statistical objectives, may be directed.

XIII. Organization for the use of penicillin: In order to make the most effective use of penicillin, it is directed that a "Penicillin Service" or "Penicillin Team" be established in each hospital receiving the drug. The medical officer to be in charge of this service and his assistants should be selected with careful consideration of their fitness for such an undertaking. The medical officer in charge should be given full responsibility for the use of penicillin in all units of the hospital. It shall be his duty to acquaint himself and his associates with all available data on the use of penicillin and to keep informed of current developments; to select cases after due consultation; to supervise administration; to observe and record results and to render the reports indicated in this letter.

XIV. Current Clinical Investigation and Research: Limited experience and research, though incomplete, have given us certain information which is, perhaps, worth recording at this time.

Prophylaxis of infection in battle wounds with penicillin powder is being studied.

Calcium penicillin, now in very limited production, promises to be of value. Local irritation, using this salt diluted with a neutral soluble powder

is very slight, while the sodium salt of penicillin in powder form is quite irritant.

The experience reported to date regarding the use of penicillin in acute and chronic pulmonary suppuration is encouraging.

Relapsing fever in laboratory animals responds sufficiently well to warrant a trial in human cases. In spite of the fact that the in vitro effect of penicillin on the anthrax bacillus is questionable, excellent results have been obtained in the treatment of some patients infected with anthrax.

Penicillin has not been shown to be effective in the treatment of malaria, tuberculosis, plague, tularemia, scrub typhus, trypanosomiasis or rickettsial infection.

A few cases of rheumatic fever have been treated with penicillin and negative results obtained. Further study is being conducted.

At this time all evidence still indicates that penicillin is without permanent beneficial effect in the therapy of subacute bacterial endocarditis.

--BuMed. Ross T. McIntire.

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BUMED-X-III-FHM
L8-2/JJ57(042-43)

7 Jan 1944

To: All Ships and Stations.

Subj: Medical Stores: Penicillin.

Ref: (a) BuMed ltr of Information and Instruction, L8-2/JJ57(042-43), 7 Jan 1944.

1. Penicillin has been added to the Supply Catalog as follows:

Stock No.	Item	Unit
S1-1130	Penicillin, sodium, crystalline, 100,000 Oxford units in ampule (5 ampules in box) (potency 3 months)	Ampule

2. Issues of limited stocks available have previously been specifically rationed. Recent production expansion has resulted in increased quantities being allocated for Navy use. Effective 1 February 1944, specific rationing of penicillin will be discontinued.

3. Penicillin is now carried in stock at NMSD, Brooklyn, N. Y. only. When anticipated increase in deliveries permit, stock will be carried at NMSDs, Oakland and Pearl Harbor, T. H. It is not expected that available production will permit stocking of penicillin at other Naval Medical Supply Depots or Storehouses, particularly in view of the short potency period.

4. After 1 February 1944, penicillin will be issued on NavMed Form 4 requisition, or despatch request when urgency warrants, to BuMed (Materiel Division, Brooklyn), for the treatment of those conditions for which the drug is known to be effective. Such requisitions or requests shall contain a concise statement as to the urgency of the need, to enable decision as to priority of issue in the event stocks are inadequate to fill all requests. Quantities requested shall be limited - to not more than one (1) month's requirements.

5. Penicillin on hand at any activity, which prospectively cannot be utilized within potency dating shall be reported as excess, by air mail or despatch to BuMed (Materiel Division, Brooklyn), not less than two (2) weeks prior to expiration dating. Such material will be ordered transferred to the nearest activity prepared to use it. --BuMed. Ross T. McIntire.

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